

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
4 January 2001 (04.01.2001)

PCT

(10) International Publication Number
WO 01/00253 A1

(51) International Patent Classification⁷: A61L 15/20, A61K 7/48, A61F 13/15, A61K 9/70

(21) International Application Number: PCT/US00/17998

(22) International Filing Date: 29 June 2000 (29.06.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/141,787 30 June 1999 (30.06.1999) US
09/571,294 12 May 2000 (12.05.2000) US

) Applicant: KIMBERLY-CLARK WORLDWIDE, INC. [US/US]; 401 N. Lake Street, Neenah, WI 54956 (US).

(72) Inventors: YAHIAOUL, Ali; 5040 Foxberry Lane, Roswell, GA 30075 (US). EVERHART, Dennis, Stein; 230 Hereford Road, Alpharetta, GA 30004 (US). MAY, Wade, Bolton; 1904 Albert Street, Alexandria, LA 71301 (US).

(74) Agents: LETSON, William, W. et al.; Kimberly-Clark Worldwide, Inc., 401 N. Lake St., Neenah, WI 54956 (US).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

- With international search report.
- Before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: DELIVERY OF A BOTANICAL EXTRACT TO A TREATED SUBSTRATE FOR TRANSFER TO SKIN

(57) Abstract: The present invention relates to a combination for surface treatment of a substrate, e.g. a nonwoven web, used in personal care product applications. The surface treatment combination not only provides adequate fluid handling properties, but also provides a topical delivery system effective in depositing a thin, tenacious and substantially continuous coating of a botanical extract on skin by an aqueous emulsion mediated dissolution of the agent from a substrate with subsequent transfer and deposition onto the skin. Coatings of the botanical extract on the skin resist removal, thereby preventing damage to the natural skin barrier and providing a protective barrier against chemically- and biochemically-induced skin damage.

WO 01/00253 A1

**DELIVERY OF A BOTANICAL EXTRACT TO A
TREATED SUBSTRATE FOR TRANSFER TO SKIN**

This application claims the benefit of U.S. Provisional Application No. 60/141,787,
5 entitled "DELIVERY OF A BOTANICAL EXTRACT TO A TREATED SUBSTRATE FOR
TRANSFER TO SKIN", filed June 30, 1999.

FIELD OF THE INVENTION

This invention relates to the use of a botanical extract to enhance skin health. A
treatment combination includes a surfactant and botanical extract that can be applied to a
10 substrate such as a nonwoven web, such that the composition will impart adequate fluid
handling properties to the substrate and will subsequently be transferred to the skin for
enhancing skin health. The treatment composition may further be used as a vehicle to
deliver other agents to the skin, e.g. proteins.

BACKGROUND OF THE INVENTION

15 The skin is naturally an excellent barrier to the penetration of many foreign
substances. From time-to-time, the natural ability of the skin to protect is compromised by
external factors including abrasions, irritants and the like. Attempts have been made in
recent years to promote skin health through the use of various products containing
additives or developing synthetic or naturally occurring polymers that mimic or
20 complement the properties of skin in order to maintain the skin health.

It is known that various agents have skin enhancing properties when applied to
skin and hair. Effective delivery of botanical extracts that can enhance or prevent damage
to the underlying protective barrier of skin, is an interest in a variety of medical as well as
personal care industries such as dermatology and cosmetics, respectively.

25 Enhancing skin health and delivering agents to the skin to promote skin health has
many advantages including: 1) protecting the skin and maintaining the skin in a moist
state, essentially free from chapping or irritation, 2) pH buffering and barrier enhancement
to maintain or enhance such base properties of skin, 3) inhibition of irritants that are
suspected to promote irritant or allergic contact dermatitis, and 4) maintaining the lubricity
30 of skin.

The permeability of the skin to a foreign substance is influenced by a combination
of physico-chemical parameters for both the therapeutic ingredient or active object and
the vehicle, if applicable, that delivers the ingredient or object. Maintaining health of the
skin and its underlying barrier properties requires optimal physico-chemical properties of
35 the skin.

Botanical extracts are well known to impart a variety of skin care attributes and are common ingredients in a number of commercially available products, but are usually delivered via a lotion, cream or foam. There remains a need for a treatment composition for use with a substrate that is capable of delivering a thin, tenacious, substantially continuous film of the botanical extract to the skin that can provide emollience, enhance skin barrier repair, prevent or reduce skin irritation, maintain pH, and maintain skin hydration and lubrication. The combination of the instant invention fulfills this need. Additionally, while skin wellness additives are known, other compositions have had the undesired side effect of reducing wettability, or the fluid intake rate, of the substrate.

There remains a need for a treatment combination for application and use with a substrate that will not adversely affect fluid properties of the substrate, e.g. fast and sustainable fluid intake rate, while delivery of the active agents is not compromised.

SUMMARY OF THE INVENTION

The present invention relates to a combination for surface treatment of a substrate, e.g. a nonwoven web, used in personal care product applications. The surface treatment combination not only provides adequate fluid handling properties, but also provides a topical delivery system effective in depositing a thin, tenacious and substantially continuous coating of a botanical extract on skin by an aqueous emulsion mediated dissolution of the agent from a substrate with subsequent transfer and deposition onto the skin. Coatings of the botanical extract on the skin resist removal, thereby preventing damage to the natural skin barrier and providing a protective barrier against chemically- and biochemically-induced skin damage. Also provided is a treatment combination for application and use with a substrate that will not adversely affect fluid properties of the substrate, e.g. fast and sustainable fluid intake rate as long as the material/product is being used.

BRIEF DESCRIPTION OF THE DRAWINGS

The file of this patent contains at least one drawing executed in color. Copies of this patent with color drawings will be provided by the Patent and Trademark Office upon request and payment of the necessary fee.

FIG. 1 is a schematic illustration of a treating process useful for application of the treatment combination of the present invention to one or both sides of the nonwoven web.

FIG. 2 is a partially cut-away top plan view of an exemplary personal care product, in this case a diaper, which may utilize the treated substrate according to the present invention.

FIG. 3 is a 200X optical microscopy (Brightfield and Fluorescent Image) of a substrate treated with a treatment composition according to an aspect of the present invention.

FIG. 4 is a 200X optical microscopy (Fluorescent Image) showing the liquid mediated transfer of the treatment composition from the treated substrate and dissolving in the liquid.

FIG. 5 is a 200X optical microscopy (Fluorescent Image) of skin that has been
5 treated with a treatment composition including liquid mediated transfer of the composition to the skin, wherein the botanical extract has been labeled with a fluorescent dye to show the transfer of a thin, tenacious, substantially continuous film to the skin.

FIG. 6 is a 100X optical microscopy (Brightfield and Fluorescent Image) of skin
10 that has been treated in accordance with the prior art in that the treatment composition has been transferred to the skin by mechanical transfer, wherein a silk protein has been labeled with a fluorescent dye to show the transfer of a substantially discontinuous film to the skin.

DETAILED DESCRIPTION OF THE INVENTION

Combinations and methods are provided by the present invention for topical
15 administration of skin treatment compositions to the skin of mammals, especially humans, to protect the skin by preserving and restoring the natural integrity of the skin. This is achieved by depositing a botanical extract from a substrate that is able to control the release of the agent to the surface of the skin. The botanical extract acts as a protectorant that is capable of maintaining the pH of the skin, inhibit the activity of irritants to the skin, and maintain skin hydration and lubrication. Pancreatic digestive enzymes
20 that are expelled by the body with feces have been implicated to induce skin inflammation (Anderson, P.H., Bucher, A.P., Saees, II, Lee, P.C., Davis, J.A., and Maibach, H.I., Faecal enzymes: in vivo skin irritation. *Contact Dermatitis* 1994; 30, 152-158). When the feces, including these enzymes, contact the skin, the skin becomes irritated. In some cases, proteases, e.g. fecal and urine proteases, cleave stratum corneum proteins, thereby
25 breaking down the natural protective barrier of the skin, and leaving the skin susceptible to irritation by enzymes. The treatment composition of the present invention is designed to form a thin, tenacious, substantially continuous film over the skin to inhibit, or at least minimize, the effect of such irritants.

30 The treatment composition of the present invention includes a surfactant and a botanical extract. Preferably, the treatment composition is prepared as an emulsion of the surfactant and botanical extract, usually as an oil-in-water (o/w) emulsion.

Examples of emulsions include aqueous emulsions of botanical extract,
(Cronatural Brazil Nut Oil DS-68R-1, Croda Inc., Parsippany, NJ), and surfactant, e.g.
35 AHCOVEL Base N-62 (hereinafter "AHCOVEL"), a mixture of sorbitan monooleate and polyethoxylated hydrogenated castor oil, manufactured by Hodgson Co. It has been

found that when emulsions containing up to about 90 wt.% surfactant and up to about 50 wt.% botanical extract at about 0.1 to 40 wt.% total solids are used, sufficient amounts of the botanical extract transfer to the skin. Preferably, the emulsions will contain between about 5 to 30 wt.% solids. These emulsions can either be applied onto a substrate from a high-solids bath (up to 40 wt.%) or from dilute baths ranging from 0.1 wt.% to about 20 wt.%. Preferably, the emulsion will be diluted to about 0.5 wt.% to about 15 wt.%. 5

The surfactants useful in the treatment composition of the present invention will provide superior fluid handling performance, skin protection and mildness to human skin. Useful examples of the surfactant include ethoxylated hydrogenated fatty oils, monosaccharides, monosaccharides derivatives, polysaccharides, polysaccharide derivatives, and combinations thereof. 10

Water miscible nonionic surfactants are preferred and such surfactants are commercially available. Examples of such surfactants include AHCOVEL and Glucocon 220UP, available from Henkel Corporation, which is an alkylpolyglycoside having 8 to 10 carbons in the alkyl chain, and may also be used as a part of the surfactant. Other well known nonionic surfactants are the primary aliphatic alcohol ethoxylates, secondary aliphatic alcohol ethoxylates, alkylphenol ethoxylates and ethylene-oxide-propylene oxide condensates on primary alkanols, such as PLURAFACS and PLURONICS (available from BASF, Inc.) and condensates of ethylene oxide with sorbitan fatty acid esters such as TWEEN (also available from Uniqema). The nonionic surfactants generally are the condensation products of an organic aliphatic or alkyl aromatic hydrophobic compound and hydrophilic ethylene oxide group. Practically any hydrophobic compound having a carboxy, hydroxy, amido, or amino group with a free hydrogen attached to the nitrogen can be condensed with ethylene oxide or with the polyhydration product thereof, polyethylene glycol, to form a water miscible nonionic surfactant. Other suitable surfactants include polyoxyethylene sorbitan monolaurate, polyoxyethylene sorbitan monostearate, polyoxyethylene sorbitan trioleate, polyoxyethylene sorbitan tristearate, and natural surfactant such as bovine lipid extract surfactant (Survanta, Ross Laboratories), a drug used to treat Acute Respiratory Distress Syndrome and Cystic Fibrosis, and enzymes such as papain or pepsin which cleave protein structures. 20 25 30

More specifically, the nonionic surfactant may include the condensation products of a higher alcohol (e.g., an alkanol containing about 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18 carbon atoms in a straight or branched chain configuration) condensed with about 5 to 30 moles of ethylene oxide. Examples include: lauryl or myristyl alcohol condensed with about 16 moles of ethylene oxide (EO); tridecanol condensed with about 6 moles of EO; myristyl alcohol condensed with about 10 moles of EO per mole of myristyl alcohol; the 35

condensation product of EO with a cut of coconut fatty alcohol containing a mixture of fatty alcohols with alkyl chains varying from 10, 11, 12, 13 or 14 carbon atoms in length and wherein the condensate contains either about 6 moles of EO per mole of total alcohol or about 9 moles of EO per mole of alcohol; and tallow alcohol ethoxylates containing 6
5 EO to 11 EO per mole of alcohol. Condensates of 2 to 30 moles of ethylene oxide with sorbitan mono- and 3C₁₀-C₂₀ alkanolic acid esters having a HLB (hydrophilic/lipophilic balance) of about 4 to 20, preferably about 8 to 15, may also be employed as the nonionic surfactant.

Another class of surfactant compounds include the alkyl polysaccharides. Alkyl
10 polysaccharides are alkyl polyglycosides having the formula SUGAR-O-R, where R is a hydrophobic group.

Turning to the botanical extract, the present invention provides enhanced skin barrier repair and moisture balance of the skin. Examples of such extracts include natural blends of fatty acids which mimic those found in the stratum corneum, mixture of fatty
15 acids with pigments such as carotenes, carotenoids or phytosterols that are known to facilitate repair to damaged skin, and the like. Specific examples of useful botanical extracts include avocado, which contains the sterol sitosterol; carrot, which contains beta carotene; sesame oil which contains a mixture of saturated and unsaturated fatty acids, and brazil nut oil. Because of its broad distribution of fatty acids, extracts such as brazil
20 nut oil, can outperform single fatty acids with respect to incorporation into the lipid lamellar structures. Brazil nut oil (BNO) originates from the harvested fruit from the South American rain forest tree: *Bertholletia excelsa*. Advantageously, the botanical extract will be present in the composition as an aqueous emulsion. However, non-aqueous blends can also be produced to impart similar attributes.

25 The amount of botanical extract will be introduced in the combination described above in the range of from about 0.01% to about 50% by weight of the composition. Preferably, the agent will be present in the amount of about 0.25% to about 2% by weight of the composition.

Compositions and methods are also provided by the present invention for topical
30 administration of the botanical extract concurrently with a protein that can be administered topically in a controlled manner.

One such protein is sericin. Sericin is one of two proteins that are part of the twin fibroin silk thread spun by *Bombyx mori*, a domestic insect. Sericin acts as a protective envelope around the fibroin thread as it is spun, which is like spinning of fibers with
35 soluble sizing agents to help form good quality fibers. The sericin can be easily separated from silk protein by hydrolysis. Post-spun sericin, with its unique properties, is known to

have high affinity to a number of proteins. When refined to a high molecular weight substance it is amenable to binding to the keratin of skin and hair, forming a resistant, moisturizing, and protective film on the skin/hair, imparting good barrier properties.

Sericin is a silk protein obtained by controlled hydrolysis of low molecular weight silk having a specific gravity of at least about 1. A commercially available silk protein is available from Croda, Inc., of Parsippany, NJ, and is sold under the trade name CROSILK LIQUID (silk amino acids), CROSILK 10,000 (hydrolyzed silk), CROSILK POWDER (powdered silk), and CROSILKQUAT (cocodimonium hydroxypropyl silk amino acid). Another example of a commercially available silk protein is SERICIN, available from Pentapharm, LTD, a division of Kordia, bv, of the Netherlands. Further details of such silk protein mixtures can be found in U.S. Patent No. 4,906,460, to Kim, et al., assigned to Sorencor, which is herein incorporated by reference in its entirety.

The silk protein derivatives may be chosen from one of several potential compositions. Included among the silk derivatives are silk fibers and hydrolysate of silk fibers. The silk fibers may be used in the form of powder in preparing the emulsion or as a powder of a product obtained by washing and treating the silk fibers with an acid. Preferably, silk fibers are used as a product obtained by hydrolysis with an acid, alkali or enzyme, as disclosed in U.S. Patent No. 4,839,168 to Abe et al.; U.S. Patent No. 5,009,813 to Watanube et al., and U.S. Patent No. 5,069,898 to Goldberg, each incorporated herein by reference in its entirety.

Another silk derivative that may be employed in the composition of the present invention is protein obtained from degumming raw silk, as disclosed, for example, in U.S. Patent No. 4,839,165 to Hoppe et al., incorporated herein by reference in its entirety. The principal protein obtained from the raw silk is sericin, which has an empirical formula of $C_{15}H_{25}O_3N_5$ and a molecular weight of about 323.5.

A preferred silk derivative is a mixture of two or more individual amino acids, which naturally occur in silk. The principal silk amino acids are glycine, alanine, serine and tyrosine.

Another example of a silk derivative for use in the emulsion composition of the present invention is a fine powder of silk fibroin in nonfibrous or particulate form, as disclosed in U.S. Patent No. 4,233,212 to Otoi et al., incorporated herein by reference in its entirety.

The fine powder is produced by dissolving a degummed silk material in at least one solvent selected from, for example, an aqueous cupriethylene diamine solution, an aqueous ammonia solution of cupric hydroxide, an aqueous alkaline solution of cupric hydroxide and glycerol, an aqueous lithium bromide solution, an aqueous solution of the

chloride, nitrate or thiocyanate of calcium, magnesium or zinc and an aqueous sodium thiocyanate solution. The resulting fibroin solution is then dialyzed. The dialyzed aqueous silk fibroin solution, having a silk fibroin concentration of from about 3 to 20% by weight, is subjected to at least one treatment for coagulating and precipitating the silk
5 fibroin, such as, for example, by the addition of a coagulating salt, by aeration, by coagulation at the isoelectric point, by exposure to ultrasonic waves, by agitation at high shear rate and the like.

The resulting product is a silk fibroin gel, which may be incorporated directly into a treatment composition or the same may be dehydrated and dried into a powder and then
10 dissolved in the treatment composition.

The silk material used to form the silk fibroin includes cocoons, raw silk, waste cocoons, raw silk waste, silk fabric waste and the like. The silk material is degummed or freed from sericin by a conventional procedure such as, for example, by washing in warm water containing a surfactant-active agent or an enzyme, and then dried. The degummed
15 material is dissolved in the solvent and preheated to a temperature of from about 60 to 95°C, preferably of from about 70 to 85°C. Further details of the process of obtaining the silk fibroin are discussed in previously referenced U.S. Patent No. 4,233,212.

In addition to the silk protein of the treatment composition of the present invention, an additional protein may be present in the amount of about 0.1 to about 4.0% by weight.
20 This additional protein may be selected from the group consisting of hydrolyzed animal collagen protein obtained by an enzymatic hydrolysis, lexeine protein, vegetal protein and hydrolyzed wheat protein and mixtures thereof.

The composition of the present invention can be in the form of an oil-in-water (o/w) emulsion or after dilution with water, with the essential ingredients being water, surfactant,
25 and/or co-surfactant.

Because the composition as prepared is an aqueous liquid formulation and since no particular mixing is required to form the o/w emulsion, the composition is easily prepared simply by combining all the ingredients in a suitable vessel or container. The order of mixing the ingredients is not particularly important and generally the various
30 ingredients can be added sequentially or all at once or in the form of aqueous emulsions of each or all of the primary surfactants and co-surfactants can be separately prepared and combined with each other. It is important to note that emulsions of, for instance, organic acid emulsions would not be acceptable for use in the present invention, since such emulsions would be a strong skin irritant and counterproductive to the intended use
35 of the present invention. The protein, when present, can be added as an aqueous emulsion thereof or can be added directly. It is not necessary to use elevated

temperatures in the formation step and room temperature is sufficient. However, higher temperatures of up to about 180°F (82.2°C), preferably 110 to 140°F (43.3 to 60°C), can also be used.

For administration to the skin of a human or other mammal, the treatment compositions will often be sterilized or formulated to contain one or more preservatives for incorporation into pharmaceutical, cosmetic or veterinary formulations. These treatment compositions can be sterilized by conventional, well-known sterilization techniques, e.g., boiling or pasteurization, without substantially adversely affecting the biological activity of the composition. The compositions may contain pharmaceutically acceptable auxiliary substances as required to approximate physiological conditions and as necessary to prepare compositions for convenient administration, such as pH adjusting and buffering agents, preservatives, and delivery vehicles. Actual methods for preparing pharmaceutically administrable compounds will be known or apparent to those skilled in the art and are described in detail in, for example, Remington's Pharmaceutical Science, supra.

Perfumes, dyes and pigments can also be incorporated into the treatment compositions of the invention. For semi-solid compositions, as would be appropriate for pastes and creams intended for topical administration, the peptone-copper complexes can be provided separately or may be compounded with conventional nontoxic carriers such as, for example, aloe vera gel, squalene, glycerol stearate, polyethylene glycol, cetyl alcohol, stearic acid, and propylene glycol, among others. Such compositions may contain about 5-100% active ingredients, more preferably about 5-25%.

The compositions formulated for administration to the skin are administered to a wearer, such as humans, with un-compromised skin or in situations where a subject is already suffering from damaged skin (e.g., peeling) due to ultraviolet or other irradiation or oxidative skin damage. The treatment compositions are administered in an amount sufficient to allow inhibition of further damage by topically administered irritating substances or other unknown irritating substances and are more effective than if the host were not treated. Amounts adequate to accomplish these effects are defined as a "therapeutically effective dose" and will vary according to the application.

In prophylactic and cosmetic applications the compositions are employed for protecting the skin from damage. Thus, the botanical extracts and/or silk proteins are administered to a host under conditions which protect the integrity of the skin, maintains physiological pH, skin hydration and lubrication. In these uses, the precise amounts again depend on the amount of protection desired and the extent and conditions under which the skin is exposed to potentially damaging conditions, such as those caused by fecal and

urine proteases, or other irritating substances. They can generally range from about 0.1 mg to about 10 mg per day per square centimeter of skin. Single or multiple administrations of the compositions can be carried out daily or over a prolonged period of time.

- 5 The silk proteins of the invention may be administered to the skin in relatively large amounts without serious side effects, although indiscriminate use may produce irritation of the skin. In instances where the compositions are administered prophylactically to inhibit oxidative or biochemical damage to the skin or to those suffering from only mild skin damage, irritation or inflammation of the skin, the dose may be adjusted to lower
- 10 maintenance levels.

- The treatment composition providing skin protection and enhanced repair of the present invention, including pharmaceutical compositions, may be administered alone or as combination or adjunct therapy or prophylaxis. For example, the treatment compositions can be used in combination with other skin protective factors or those found
- 15 to improve other aspects of protection or healing. In this manner a synergistic effect may be attained that yields a clinical efficacy greater than that realized with any single factor.

 Further, while the compositions described herein stimulate a spectrum of skin protective processes, skin can differ considerably in its properties, leading one to utilize a combination of a composition described herein and another compound or factor.

- 20 Factors with reported healing properties which can be included with the silk protein compositions for use in protective/healing formulations and methods of the present invention include, for example, epidermal growth factor, fibroblast growth factor, nerve growth factor, transforming growth factors, angiogenic growth factors, heparin, fibronectin, fibrin, platelet-derived growth factor, enzymatic superoxide dismutase, extracts of blood or
- 25 factors from the blood, and other similar factors.

- Substrates particularly adapted to receive exudate liquids such as menses, mucous, blood products, urine, feces, and others, which will be apparent to those skilled in the art, are useful in the present invention. As used herein, the term "substrate" refers to a material that can be a woven fabric, knit fabric, nonwoven fabric, foam, film-like
- 30 material (e.g. an apertured film-like material) or paper material. Particularly useful substrates include infant and child care products such as disposable diapers, training pants and baby wipes, feminine hygiene products such as menses absorbing devices like sanitary napkins and tampons, wound dressings, bandages, and incontinence products, for example. In accordance with the invention the substrate is often normally hydrophobic
- 35 and contains a treatment composition placed so as to contact the exudate. Many polymers useful in the formation of nonwoven webs, e.g. polypropylene, are hydrophobic

and highly apolar. As is known to those skilled in the art, sericin is highly hydrophilic, hence it is polar. There is, therefore, no affinity between the substrate and the silk protein, making it difficult to apply the silk protein to the substrate. In one aspect of the invention, the unique combination of the silk protein with the surfactant and botanical
5 extract of the present invention overcomes this lack of affinity. In other words, the surfactant serves as a medium to carry the silk protein for application to the substrate. As would be understood by those skilled in the art, some synthetic fibers, such as nylon, are hydrophilic, and would not therefore have this particular problem addressed with the present invention.

10 Advantageously the substrate is a nonwoven web and may be, for example, a spunbond, meltblown, coformed or bonded carded web. Additional substrates which can be used include foams and films that are fibrillated, apertured or otherwise treated to have fiber-like properties as well as laminates of these and/or nonwoven webs. Depending on the particular application, the substrate may be used as a body contact liner, a distribution
15 layer between a liner and an absorbent layer, an absorbent layer, or in more than one of these layers.

As used herein the term "nonwoven fabric or web" means a web having a structure of individual fibers or threads, which are interlaid, but not in a regular or identifiable manner as in a knitted fabric. The term also includes individual filaments and strands, yarns or tows
20 as well as foams and films that have been fibrillated, apertured, or otherwise treated to impart fabric-like properties. Nonwoven fabrics or webs have been formed from many processes such as for example, meltblowing processes, spunbonding processes, coforming processes and bonded carded web processes. The basis weight of nonwoven fabrics is usually expressed in ounces of material per square yard (osy) or grams per square meter
25 (gsm) and the fiber diameters useful are usually expressed in microns. (Note that to convert from osy to gsm, multiply osy by 33.91).

As used herein the term "microfibers" means small diameter fibers having an average diameter not greater than about 50 microns, for example, having an average diameter of from about 0.5 microns to about 50 microns, or more particularly, microfibers
30 may have an average diameter of from about 2 microns to about 40 microns. Another frequently used expression of fiber diameter is denier, which is defined as grams per 9000 meters of a fiber and may be calculated as fiber diameter in microns squared, multiplied by the density in grams/cc, multiplied by 0.00707. A lower denier indicates a finer fiber and a higher denier indicates a thicker or heavier fiber. For example, the diameter of a
35 polypropylene fiber given as 15 microns may be converted to denier by squaring, multiplying the result by 0.89 g/cc and multiplying by 0.00707. Thus, a 15 micron polypropylene fiber

has a denier of about 1.42 ($15^2 \times 0.89 \times 0.00707 = 1.415$). Outside the United States the unit of measurement is more commonly the "tex", which is defined as the grams per kilometer of fiber. Tex may be calculated as denier/9.

As used herein the term "spunbonded fibers" refers to small diameter fibers which are formed by extruding molten thermoplastic material as filaments from a plurality of fine, usually circular capillaries of a spinneret with the diameter of the extruded filaments then being rapidly reduced as, for example, described in U.S. Patent No. 4,340,563 to Appel et al., and U.S. Patent No. 3,692,618 to Dorschner et al., U.S. Patent No. 3,802,817 to Matsuki et al., U.S. Patent Nos. 3,338,992 and 3,341,394 to Kinney, U.S. Patent No. 3,502,763 to Hartmann, U.S. Patent No. 3,502,538 to Levy, and U.S. Patent No. 3,542,615 to Dobo et al. Spunbond fibers are quenched and generally not tacky when they are deposited onto a collecting surface and usually subjected to a separate bonding step. Spunbond fibers are generally continuous and have average diameters frequently larger than 7 microns, more particularly, between about 10 and 20 microns.

As used herein the term "meltblown fibers" means fibers formed by extruding a molten thermoplastic material through a plurality of fine, usually circular, die capillaries as molten threads or filaments into converging high velocity, usually heated, gas (e.g. air) streams which attenuate the filaments of molten thermoplastic material to reduce their diameter, which may be to microfiber diameter. Thereafter, the meltblown fibers are carried by the high velocity gas stream and are deposited on a collecting surface often while still tacky to form a web of randomly dispersed meltblown fibers. Such a process is disclosed, for example, in U.S. Patent No. 3,849,241 to Butin. Meltblown fibers are microfibers which are usually continuous, but which may also be discontinuous, and are generally smaller than 10 microns in average diameter.

The substrate of the present invention may also include a bonded carded web. As used herein "bonded carded webs" or "BCW" refers to nonwoven webs formed by carding processes as are known to those skilled in the art and further described, for example, in coassigned U.S. Patent No. 4,488,928 to Alikhan and Schmidt which is incorporated herein by reference in its entirety. Briefly, carding processes involve starting with a blend of, for example, staple fibers with bonding fibers or other bonding components in a bulky batt that is combed or otherwise treated to provide a generally uniform basis weight. This web is heated or otherwise treated to activate the adhesive component resulting in an integrated, usually lofty nonwoven material.

As would be understood by one of ordinary skill in the art, such nonwoven webs may be formed from different types of polymers, which may be extruded as monocomponent fibers, biconstituent fibers and/or conjugate fibers (multi- and bicomponent fibers) filaments.

Biconstituent fibers are sometimes also referred to as multiconstituent fibers. Fibers of this general type are discussed in, for example, U.S. Patent No. 5,108,827 to Gessner. Bicomponent and biconstituent fibers are also discussed in the textbook Polymer Blends and Composites by John A. Manson and Leslie H. Sperling, copyright 1976 by Plenum Press, a division of Plenum Publishing Corporation of New York, ISBN 0-306-30831-2, at pages 273 through 277. Conjugate fibers are taught in U.S. Patent No. 5,108,820 to Kaneko et al., U.S. Patent No. 5,336,552 to Strack et al., and U.S. Patent No. 5,382,400 to Pike et al.

Small amounts of additives may be added for color, anti-static properties, lubrication, hydrophilicity, antibacterial, antimold, deodorizing effect, and the like. These additives, e.g. titanium dioxide for color and chitosan as an antibacterial, are generally present in an amount less than 5 weight percent and more typically about 2 weight percent.

As used herein, the term "personal care product" includes diapers, training pants, swim pants, absorbent underpants, adult incontinence products, sanitary wipes, feminine hygiene products such as sanitary napkins and tampons, wound dressings and bandages.

As used herein, the term "hydrophilic" means that the polymeric material has a surface free energy such that the polymeric material is wettable by an aqueous medium, i.e. a liquid medium of which water is a major component. The term "hydrophobic" includes those materials that are not hydrophilic as defined. Hydrophobic materials may be treated internally or externally with surfactants and the like to render them hydrophilic.

The substrate of the present invention may be a multilayer laminate. An example of a multilayer laminate is an embodiment wherein some of the layers are spunbond and some meltblown such as a spunbond/meltblown/spunbond (SMS) laminate as disclosed in U.S. Patent No. 4,041,203 to Brock et al., U.S. Patent No. 5,169,706 to Collier, et al, and U.S. Patent No. 4,374,888 to Bornslaeger. Such substrates usually have a basis weight of from about 0.1 to 12 osy (6 to 400 gsm), or more particularly from about 0.75 to about 3 osy.

Spunbond nonwoven fabrics are generally bonded in some manner as they are produced in order to give them sufficient structural integrity to withstand the rigors of further processing into a finished product. Bonding can be accomplished in a number of ways such as hydroentanglement, needling, ultrasonic bonding, adhesive bonding, stitchbonding, through-air bonding and thermal bonding such as calendering.

The addition of the treatment composition to the substrate may be accomplished by conventional means such as spraying, coating, dipping and the like although the use of high solids spray is advantageous in cases where drying and/or compression is desired to be minimized. The amount of the treatment composition used will depend on the

particular end use as well as factors such as basis weight and porosity of the substrate. Referring to FIG. 1, an exemplary process will be described for application to one or both sides of a traveling substrate. It will be appreciated by those skilled in the art that the invention is equally applicable to inline treatment or a separate, offline treatment step.

- 5 Substrate 12, for example a spunbond or meltblown nonwoven web is directed over support rolls 15,17 to a treating station including rotary spray heads 22 for application to one side 14 of web 12. An optional treating station (shown in phantom) which may include rotary spray heads 18 can also be used to apply to opposite side 23 of substrate 12. Each treatment station receives a supply of treatment composition 30 from a reservoir (not shown). The
- 10 treated substrate may then be dried if needed by passing over dryer cans 25 or other drying means and then wound as a roll or converted to the use for which it is intended. Alternative drying means include ovens, through air dryers, infra red dryers, air blowers, and the like.

- As referred to above, a unique and surprising aspect of the present invention includes the ability of the treatment composition to be transferred from the substrate to the
- 15 skin. It has been found that when a liquid is introduced to the substrate, the treatment composition will dissolve in the liquid, and then liquid-mediated transfer of the treatment composition to the skin occurs. In other words, the treatment composition including the botanical extract dissolves off of the substrate into the liquid, which then deposits the thin, tenacious and substantially continuous film of the botanical extract onto the skin. Urine is
- 20 an example of a liquid that can transfer the treatment composition from the substrate to the skin. As another example, the liquid generated by the body after abrasion or injury to the skin, might provide sufficient liquid-mediated transfer of the treatment composition from the substrate, in this case, a bandage or wound dressing. In general, when wetness increases, the treatment composition will transfer to the skin to form a protective barrier.

- 25 An exemplary article 80, in this case a diaper, is shown in FIG. 2. Referring to FIG. 2, most such personal care absorbent articles 80 include a liquid permeable top sheet or liner 82, a barrier back sheet or outercover 84 and an absorbent core 86 disposed between and contained by the top sheet 82 and back sheet 84. Articles 80, such as diapers, may also include some type of fastening means 88 such as adhesive fastening
- 30 tapes or mechanical hook and loop type fasteners to maintain the garment in place on the wearer. The substrate 12 may be used to form various portions of the article including, but not limited to the top sheet or liner 82.

The following examples are offered by way of illustration, not by way of limitation.

EXAMPLES

- 35 The compositions of the present invention were formed by creating an emulsion of a botanical extract and water as the carrier liquid. Aqueous emulsions of brazil nut oil as

the botanical extract, AHCOVEL, as the surfactant system, and, in some instances, SERICIN and CROSILK as the silk protein, were prepared. The stable emulsions were diluted to about a 5% by weight solids and applied to the surface of a polyolefin nonwoven liner fabric at about 0.3 to 6% by weight via a saturation dip and squeeze process as described in more detail below. The fabrics were then tested for fluid intake rate, softness, skin transfer, skin barrier, and the like, as describe in more detail below.

Fluid Intake Rate: This test is identified as Fluid Strikethrough EDANA 150.1-90 and measures the time taken for a known volume of liquid (simulated urine) applied to the surface of a nonwoven test sample in contact with an underlying absorbent pad to pass through the nonwoven. In general, a 50 ml burette is positioned on a ring stand with the tip inside a funnel. A standard absorbent pad of 5 plies of specified filter paper (482% absorbency) is placed on an acrylic glass base plate below the funnel, and a nonwoven sample is placed on top of the absorbent. An acrylic glass strike-through plate 25 mm thick and weighing 500 g is placed over the sample with the cavity centered 5 mm below the funnel. The burette is filled with liquid, keeping the funnel closed, and a quantity of the liquid (e.g., 5 ml or 10 ml) is run into the funnel. The 5 ml or 10 ml is allowed to discharge starting a timer which stops when the liquid has penetrated into the pad and fallen below a set of electrodes, and the elapsed time is recorded. The liquid used was Blood Bank Saline, available from Stephens Scientific Co., Catalog No. 8504.

Softness Test: A sensory panel was assembled to review softness of substrates including combinations of surfactant and BNO, as well as a control substrate. Approximately 5 panelists reviewed the substrates and rated the substrates on a scale of 1 to 3, with the higher number indicating improved perceived softness. The results of the test are provided below.

Skin Transfer Test: BNO was mixed with the fluorescent dye, BODIPY[®] dodecanoic acid available from Molecular Probes, Inc., Eugene OR (Catalog No. D-3823). Sericin was labeled with Texas Red (TR) according to the procedure outlined by Molecular Probes, Inc. (Molecular Probes labeling kit F-6112) Texas Red protein labeling kit F-6162). A 4.5 wt.% emulsion of sericin, 200uL, was reacted with 100uL of a 5mg/mL solution of Texas Red succinimide in dimethylsulfoxide for 1 hour. The thus labeled extract was isolated via gel chromatography with centrifugation for 3 minutes at 1100 times the force of gravity.

Emulsions of AHCOVEL containing a mixture of TR labeled sericin or BNO containing the fluorescent additive was used to treat a substrate of 0.6 osy polypropylene spunbond nonwoven web, prepared as a diaper liner according to the procedure described. Fluorescent microscopy confirmed the presence of the BNO on the skin.

Additionally, a composition of AHCOVEL and silk protein was prepared and labeled as described above. Again, fluorescent microscopy using a high pressure Hg lamp with excitation and emission bandpass filters of 595nm and 615nm, respectively, confirmed the presence of the labeled protein on the substrate. FIG. 3 is a 200X optical microscopy (Brightfield and Fluorescent Image) of the substrate treated with the treatment composition according to the present invention. The untreated substrate showed no significant fluorescence, (not shown).

Upon exposing the treated substrate to water, intense fluorescence, characteristic of TR, could be detected in solution, suggesting solubility of the labeled protein into the wetting media. Sericin was removed from the substrate due to its solubility in water. FIG. 4 is a 200X optical microscopy (Fluorescent Image) showing this liquid mediated transfer of the treatment composition from the treated substrate and dissolving in the liquid.

Transfer of the labeled protein from the treated substrate to the skin was verified by the following procedure. A 1 cm² square of treated substrate was secured to the volar forearm with adhesive tape. A majority of the area of the substrate was not covered with tape, which was placed only on the perimeter to secure the substrate to the arm. The substrate was subsequently wetted with 300uL of water. After several minutes, the substrate was removed from the arm, and the stratum corneum previously covered by the material was tape stripped with Dsquake tape to remove superficial layers of skin for fluorescent microscopic analysis. Microscopy at 100x and 200x clearly revealed intense fluorescence associated with the TR labeled protein, thus confirming that transfer from the substrate to the skin, mediated by wetting, was conclusive. FIG. 5 shows the thin, tenacious, substantially continuous film of silk protein that was applied to the skin by means of the present invention. The morphology of the resulting protein coating was consistent with a thin, tenacious, substantially continuous film of the sericin protein on the corneocytes of the forearm. FIG. 6, on the other hand, shows the variability of application of the silk protein by means of mechanical transfer described in the prior art.

Skin Barrier Test: Uniformity of the barrier film on the skin as shown in FIG. 5 was indicative of good barrier properties.

30

Treatment compositions

Treatment compositions containing water, AHCOVEL, CROSILK, and Brazil Nut Oil, were prepared according to Table 1 below. For comparison purposes, a control composition was prepared containing only water and AHCOVEL.

35

Table 1 – Composition Concentrations (wt.%)

Compositions	Water	AHCOVEL	CROSILK	BNO
Control	80	20	-	-
1	70	20	-	10
2	70	20	5	5

Although not specifically shown in the data, silk protein emulsions, without the aid of surfactant, were applied to a substrate. Since the protein is hydrophilic, and the substrate is hydrophobic, the protein would not easily wet and saturate the substrate, and instead formed a bead on top of the substrate.

Treated Substrate

Untreated polypropylene spunbond materials (basis weight of about 0.5 ounces per square yard) were used as a substrate for the treatment compositions. The compositions were applied to the substrates by a low-solids batch treatment process. An 8 in. x 12 in. (20.32 x 30.48 cm) example of the substrate was first dipped in an aqueous treatment bath of known composition illustrated in Table 2 below.

The saturated examples were then nipped between two rubber rollers in a laboratory wringer, Type LW-1, No. LW-83A (Atlas Electric Devices, Chicago, IL), and subsequently dried in an oven at 60°C for about 20 minutes or until constant weight was obtained. Nip pressure was adjusted to achieve a 100% wet pick-up (%WPU). %WPU is calculated from the following equation:

$$\%WPU = [(W_w - W_d) / W_d] \times 100,$$

where:

Ww = wet weight of the nipped fabric,

Wd = dry weight of the treated fabric.

Knowing the bath concentration and the %WPU, the % Add On can be calculated from the following equation:

$$\%AddOn = (\%BathConcentration) \times (\%WPU) \div 100$$

If, as in this example, the %WPU = 100, then the % Add-On will equal the % Bath Concentration. However, other %WPU and % Bath Concentration combinations can be used to achieve similar results. Final % Add-On for each component of each sample is shown in the Table below.

The Fluid Intake Rate was determined for each of the examples, according to the test as described above. As shown in the data, fluid-intake rates have not been adversely affected by addition of the treatment composition of the present invention, and the substrates, therefore, provide adequate fluid handling properties. A typical liner treated

with AHCOVEL/BNO has shown good fluid handling properties on multiple fluid insults as well as an ability to transfer BNO to skin, providing measurable emollience.

Table 2 - Fluid Intake Time (sec.)

Ex. #	Composition	Chemical Ratio	Add-On wt. %	Intake Time (second)				
				Insult 1	Insult 2	Insult 3	Insult 4	Insult 5
1	AHCOVEL	1	0.3	2.74	2.87	2.87	2.90	2.85
2			0.6	2.93	2.86	2.86	2.86	2.92
3			1	2.88	2.93	2.62	2.75	2.81
4			2	2.84	2.94	2.93	2.73	2.86
5	AHCOVEL /BNO	9/1	0.3	3.20	3.17	3.14	3.15	3.12
6			0.6	2.97	3.10	3.37	2.99	3.21
7	AHCOVEL /BNO	8/2	0.3	3.11	3.13	3.14	3.15	3.12
8			0.6	3.18	2.84	2.95	2.98	2.93
9	AHCOVEL /BNO	7/3	0.3	2.91	3.05	3.00	2.98	3.20
10			0.6	2.96	2.98	2.84	2.91	2.88
11	AHCOVEL /BNO	1/1	0.3	3.27	3.24	3.48	3.65	3.69
12			0.6	3.81	3.88	3.71	3.78	3.66
13	AHCOVEL /BNO	2/1	3	2.57	2.39	2.47	3.51	3.35
14			6	2.35	2.33	2.35	2.56	2.67
15	Control	untreated		>20	-	-		

- 5 As shown below in Table 3, a sensory panel was assembled and given an opportunity to review examples made according to Examples 13-15 above. The sensory panel perceived the substrates including the treatment composition of the present invention as softer than the untreated substrate.

Table 3

Example	Sensory Panel Softness (1 to 3)**
13	3
14	3
15	1

** Higher number indicates improved softness

While various patents and other reference materials have been incorporated herein by reference, to the extent there is any inconsistency between incorporated material and that of this written specification, the written specification shall control. In addition, while the present invention has been described in connection with certain preferred embodiments, it is to be understood that the subject matter encompassed by way of the present invention is not to be limited to those specific embodiments. On the contrary, it is intended for the subject matter of the invention to include all alternatives, modifications and equivalents as can be included within the spirit and scope of the following claims.

We Claim:

1. A treatment combination for imparting a liquid-mediated transfer medium to a substrate, said combination comprising a surfactant and a botanical extract;
the surfactant including a compound selected from the group comprising ethoxylated hydrogenated fatty oils, monosaccharides, monosaccharide derivatives,
5 polysaccharides, polysaccharide derivatives and combinations thereof.
2. The treatment combination of Claim 1, wherein said botanical extract is selected from the group comprising avocado, carrot, sesame oil and brazil nut oil.
3. The treatment combination of Claim 1, said surfactant and botanical extract are combined in an aqueous emulsion to form a treatment composition
4. The treatment combination of Claim 3, wherein said surfactant and botanical extract form a treatment composition and are present at a weight ratio of about 0.01-50 wt.% botanical extract to about 50-99.99 wt.% surfactant.
5. The treatment combination of Claim 4, wherein said emulsion further comprises 0.1 to 40 wt.% total solids.
6. The treatment composition of Claim 5 further comprising a protein.
7. The treatment composition of Claim 6 wherein said protein further comprises a silk protein.
8. A substrate treated with a treatment combination, said treatment combination comprising a surfactant and a botanical extract;
the surfactant including a compound selected from the group consisting of ethoxylated hydrogenated fatty oils, monosaccharides, monosaccharides derivatives,
5 polysaccharides, polysaccharide derivatives, and combinations thereof,
wherein said surfactant is a liquid-mediated transfer medium for transfer of said botanical extract from said substrate to a wearer.
9. The treated substrate of claim 8 wherein said botanical extract is selected from the group comprising avocado, carrot, sesame oil and brazil nut oil.

10. The treated substrate of Claim 8, wherein the substrate is selected from woven fabrics, knit fabrics, nonwoven fabrics, foams, film-like materials and paper materials.
11. The treated substrate of Claim 10, wherein the substrate comprises a nonwoven web.
12. The treated substrate of Claim 11 wherein said nonwoven web is hydrophobic.
13. The treated substrate of Claim 12, wherein said nonwoven web comprises a spunbond web, meltblown web, coformed web or bonded carded web.
14. The treated substrate of Claim 13, wherein said substrate comprises a multilayer laminate.
15. The treated substrate of Claim 8, wherein the treatment combination further comprises a protein.
16. The treatment combination of Claim 15 wherein said protein further comprises a silk protein.
17. The treated substrate of Claim 16, wherein the combination is applied at a level of about 0.1-1.5% by weight surfactant relative to the basis weight of the substrate.
18. The treated substrate of Claim 16, wherein the combination is applied at a level of about 0.1-1.0% by weight surfactant relative to the basis weight of the substrate.
19. The treated substrate of Claim 16, wherein the combination is applied at a level of about 0.1-0.5% by weight surfactant relative to the basis weight of the substrate.
20. A personal care product comprising the treated substrate of Claim 11.
21. The personal care product of Claim 20, wherein the personal care product is selected from a diaper, training pant, absorbent underpant, adult incontinence product, sanitary wipe, feminine hygiene product, wound dressing and bandage.

22. The treated substrate of Claim 11, wherein a fluid intake rate of said substrate is not adversely affected by addition of said treatment combination.

23. The method of transferring a thin, tenacious, substantially continuous film of botanical extract to skin comprising:

- a) providing a substrate;
- b) applying a treatment composition to said substrate, said composition comprising a surfactant and a botanical extract in combination; the surfactant including a compound selected from the group consisting of ethoxylated hydrogenated fatty oils, monosaccharides, monosaccharide derivatives, polysaccharides, polysaccharide derivatives, and combinations thereof,
- c) insulting said substrate with an aqueous based liquid whereby said treatment composition dissolves in said liquid, and
- d) transferring said treatment composition from said substrate to the skin, thereby forming a thin, tenacious, substantially continuous, film on the skin.

24. The method of Claim 23 wherein said substrate is a hydrophobic nonwoven web.

25. The method of Claim 23, wherein the substrate comprises a personal care product.

26. The method of Claim 23 wherein said botanical extract is selected from the group comprising avocado, carrot, sesame oil and brazil nut oil.

27. The method of claim 23 wherein said aqueous based liquid is urine.

28. The method of claim 23 wherein said aqueous based liquid is menses.

29. The method of claim 23 wherein said aqueous based liquid is sweat.

30. The method of Claim 23 further comprising addition of a protein to said substrate.

31. The method of Claim 30 wherein said protein further comprises a silk protein.

1/6

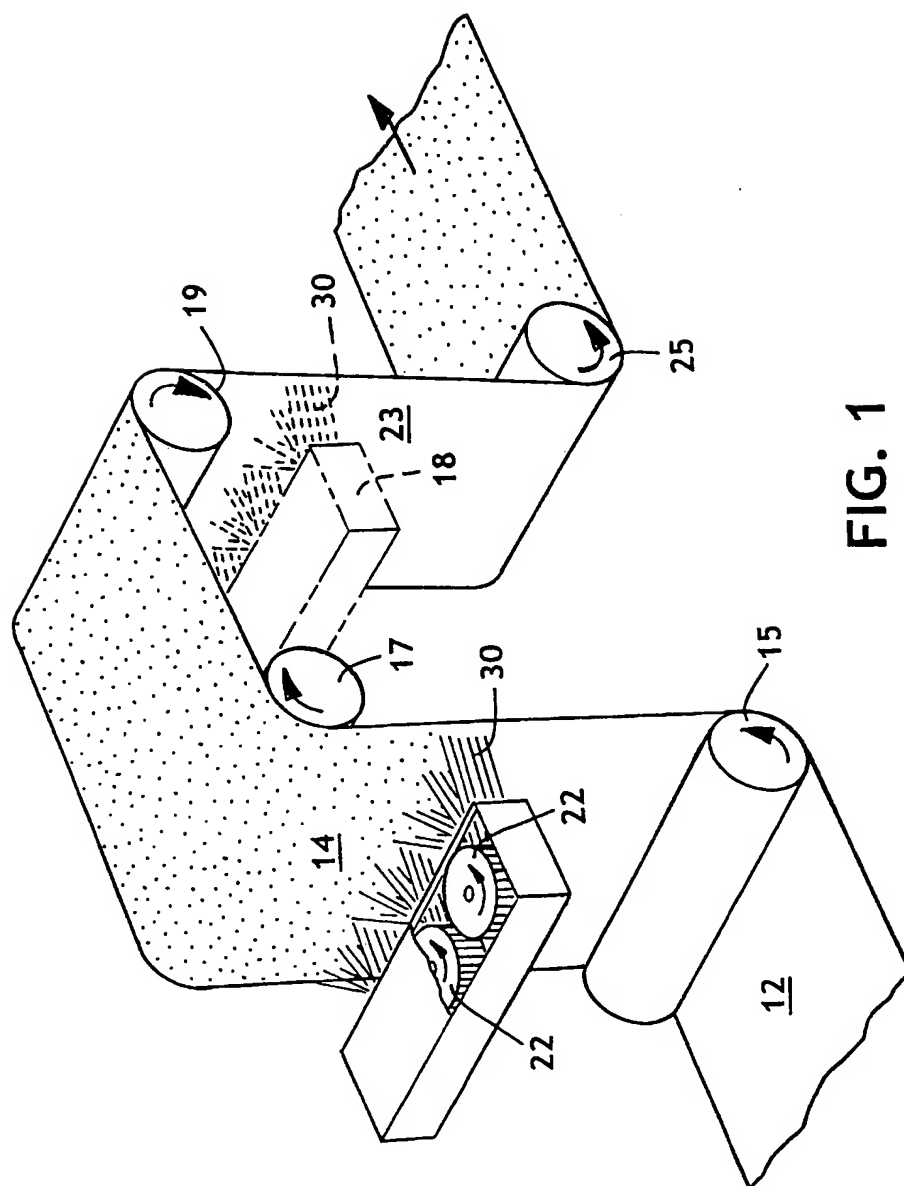


FIG. 1

2/6

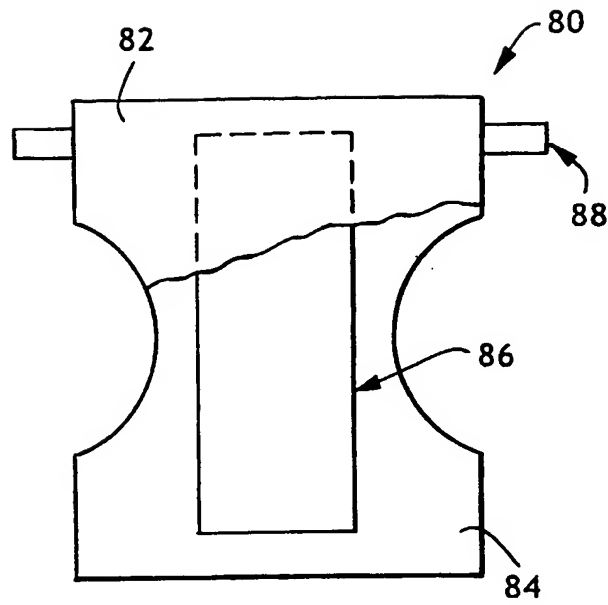


FIG. 2

3/6

Sericin Treated Nonwoven
(a) Brightfield and (b) Fluorescent Image, both at 200x

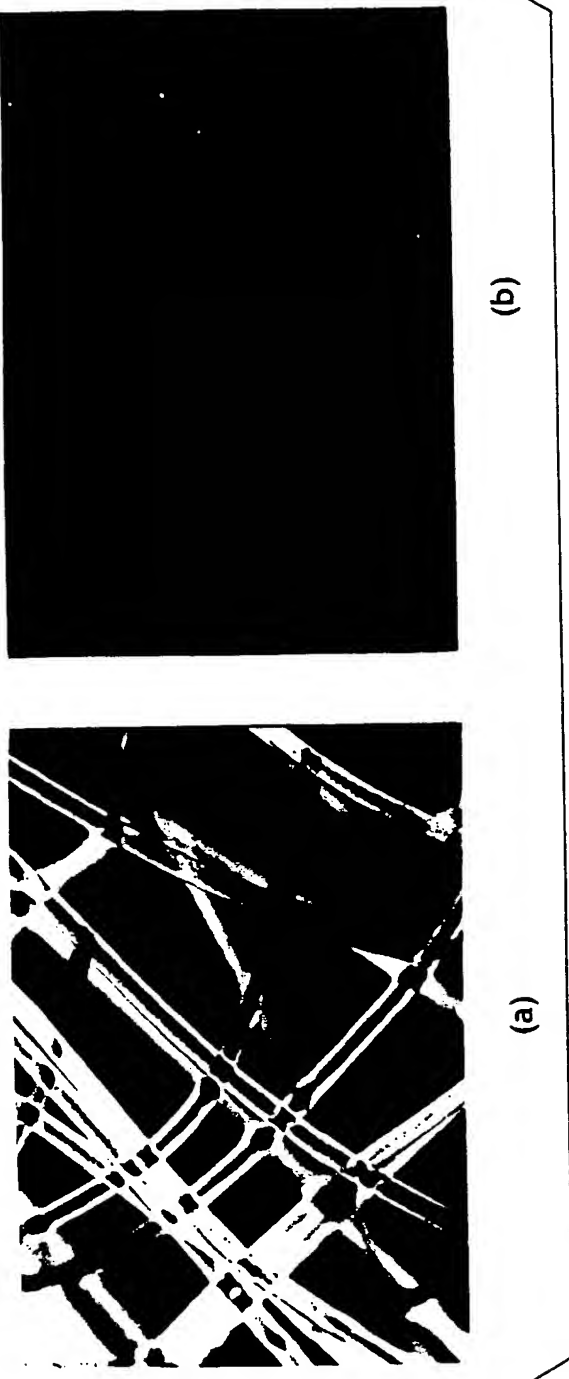
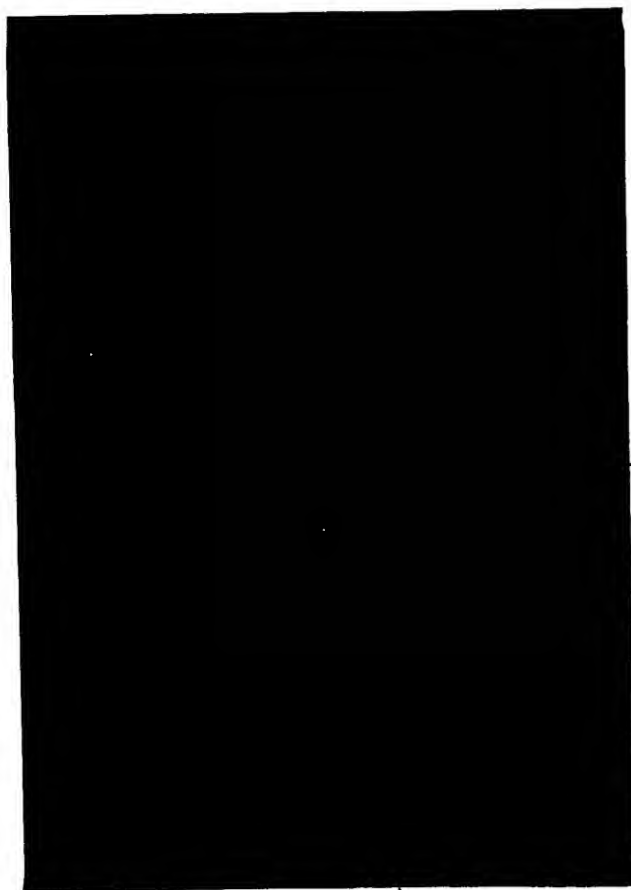


FIG. 3

4/6

Fluid Mediated Transfer of Sericin
Dissolution of Sericin from Nonwoven into Wetting Fluid



Treated Fiber

Fluid Front Containing Fluorescent Sericin

FIG. 4

5/6

Skin Coated with Sericin



FIG. 5

6/6

Dry Transfer of Sericin to Skin
(a) Brightfield and (b) Fluorescent Image, both 100x



Localized Deposition of Sericin

FIG. 6

INTERNATIONAL SEARCH REPORT

Internat. Application No
PCT/US 00/17998

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61L15/20 A61K7/48 A61F13/15 A61K9/70

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61L A61K A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	DE 199 03 717 A (HENKEL KGAA) 3 August 2000 (2000-08-03) the whole document	1
X	EP 0 842 606 A (THE PROCTER & GAMBLE CO.) 20 May 1998 (1998-05-20) the whole document	1
X	US 5 795 573 A (L. PARADISE) 18 August 1998 (1998-08-18) claims 1,2; example 2	1
A	WO 99 17738 A (LAVIPHARM LAB., INC.) 15 April 1999 (1999-04-15) claims 1,8,17	1

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

31 October 2000

Date of mailing of the international search report

10/11/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Glikman, J-F

INTERNATIONAL SEARCH REPORT

Interns 31 Application No
PCT/US 00/17998

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE 19903717 A	03-08-2000	WO 0044343 A	03-08-2000
EP 842606 A	20-05-1998	AT 190469 T	15-04-2000
		AU 5252298 A	03-06-1998
		BR 9712949 A	20-06-2000
		CN 1244893 A	16-02-2000
		DE 69607178 D	20-04-2000
		ES 2143172 T	01-05-2000
		GR 3032827 T	30-06-2000
		NO 992267 A	12-07-1999
		PT 842606 T	31-08-2000
		WO 9821307 A	22-05-1998
		US 6114298 A	05-09-2000
US 5795573 A	18-08-1998	NONE	
WO 9917738 A	15-04-1999	AU 9787398 A	27-04-1999
		EP 1024788 A	09-08-2000